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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,667	04/05/2005	Vasulinga Ravikumar	ISIS-5582	4970

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EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	**PAPER NUMBER**
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,667	RAVIKUMAR ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 11-23* is/are pending in the application.

4a) Of the above claim(s) *19 and 21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,11-18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection or objection not reiterated in this Action is withdrawn.

Election/Restrictions

Claims 19-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 18, 2006.

Claim Rejections - 35 USC § 102

Claims 1, 2, 4, 11-16 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Cook (US 5,521,302, of record).

Claim 1 is drawn to an oligomeric compound having the structure shown in the claim, having a phosphorothioate monoester at the 5' terminus wherein when Q_2 is S, Q_3 is OH or CH_3 but Q_3 must be CH_3 when Q_2 is O. Claim 2 recites that Q_1 is S, reciting a thiophosphate attached to a normal ribose sugar. Claim 4 recites that Q_3 is CH_3. Claim 11 limits claim 1 by stating that R_1, R_2 and R_3 are each H while in claim 12 they are each OH. Claim 13 limits claim 1 by stating at least one of R_1, R_2 or R_3 may be an optionally protected substituent group, while claim 14 requires at least one optionally protected substituent group. Claim 15 limits claim 1 by stating that each X_2 is S. Claim 16 limits claim 1 by reciting several possible heterocyclic base moieties that may exist

within the oligomeric compound. Claim 20 is drawn to a composition comprising the oligomeric compound of claim 1 with a pharmaceutically acceptable carrier or diluent.

Cook discloses a method of producing oligonucleotides with chirally pure phosphorus linkages using synthons that contain optionally substituted phosphate groups. The structure of the synthons used in the invention are shown in columns 4-7 and include the option that the phosphate is a phosphorothioate if one of R_d or R_e is S or the phosphate is a methyl phosphorothioate if R_e is S and R_d is methyl, the heterocyclic base can be natural or synthetic (B_x is one of the moieties listed at column 6, lines 33-36), the nucleotides can be DNA nucleotides (R_x is H) or can be RNA, possibly containing sugar substituents (R_x is OH or "a sugar derivatizing group). This structure meets the limitations of claims 11-14 and 16. Use of the disclosed synthons to produce oligonucleotides is illustrated in scheme 1. The synthons contain phosphate groups attached to the 5' hydroxyl of the sugar. Cook specifically contemplates the production of oligonucleotides containing 5' phosphate groups at column 16, lines 49-51.

The structure disclosed by Cook as structure 17 where the final R_e is S, the final R_d is methyl, at least one of the other R_d or R_e is S, R_x is H and n is 4 or more would upon removal from the CPG support produce an oligonucleotide identical to that of claims 1 and 2 where T_2 is H, T_1 is the modified phosphate group with Q_1 being S and Q_3 being CH_3, each R_1, R_2, R_3 is H and at least one of X_1 is S.

The structure disclosed by Cook as structure 17 where the final R_e is S, the final R_d is methyl, at least one of the other R_d and each of the other R_e is S and n is 4 or more would upon removal from the CPG support produce an oligonucleotide identical to

that of claim 15 where T_2 is H, T_1 is a phosphorothioate monoester with Q_1 being S and Q_3 being CH_3, and each of X_2 is S. Use of one synthon having R_x as a sugar derivatizing group produces an oligonucleotide that meets the limitations of claim 14.

Thus, Cook discloses all limitations of and anticipates claims 1, 2, 4, 11-16 and 20.

Response to arguments regarding Cook

Applicants argue the claims as amended are not anticipated by Cook. The claims now require that when Q_2 is O, Q_3 is CH_3. Q_1 and Q_3 are the equivalent of R_e and R_d in the oligonucleotides of Cook and R_d is disclosed at column 4 as including methyl. Therefore, the oligonucleotides disclosed by Cook anticipate the claims even as amended.

Claims 1-4, 11-18 and 20 rejected under 35 U.S.C. 102(b) as being anticipated by Uhlmann et al. (US 6,033,909, of record).

Claim 1 is drawn to an oligomeric compound having the structure shown in the claim, having a phosphorothioate monoester at the 5' terminus wherein when Q_2 is S, Q_3 is OH or CH_3 but Q_3 must be CH_3 when Q_2 is O. Claim 2 recites that Q_1 is S, reciting a thiophosphate attached to a normal ribose sugar. Claim 3 recites that Q_2 is S, reciting a phosphate attached to a 5'- or 3'-thionucleotide. Claim 4 recites that one position of the modified phosphate is methylated. Claim 11 limits claim 1 by stating that R_1, R_2 and R_3 are each H, while in claim 12 they are each OH. Claim 13 limits claim 1 by stating at least one of R_1, R_2 or R_3 may be an optionally protected substituent group, while claim

14 requires at least one optionally protected substituent group. Claim 15 limits claim 1 by stating that each X_2 is S. Claim 16 limits claim 1 by reciting several possible heterocyclic base moieties that may exist within the oligomeric compound. Claims 17 and 18 limit claim 1 by stating the length of the oligonucleotide is between 8 and 30 or 15 and 25. Claim 20 is drawn to a composition comprising the oligomeric compound of claim 1 with a pharmaceutically acceptable carrier or diluent.

Uhlmann et al. disclose oligonucleotides having the formula shown in claim 1. In this formula, the internucleotide linkages can be mono- or diphosphorothioate, meeting the specific limitations of claims 1 and 15. The V at the 5' position of the ribose can be O or S and the terminal R^1 can be a phosphate or thiophosphate group, which is the equivalent of the structures of claims 1-3 wherein T_1 is a modified phosphate and one of Q_1 and Q_2 is S. The Z position of the terminal phosphate groups can be C_1-C_{18} alkyl, meeting the limitation of claim 4. In the oligonucleotides disclosed by Uhlmann et al., R^2 can be hydrogen, hydroxyl or other substituents, meeting the limitations of claims 11-14. Position B is disclosed as being a conventional nucleotide base, meeting the limitations of claim 16. The oligonucleotides of Uhlmann et al. are 2-101 nucleotides in length, meeting the limitations of claims 17 and 18 and are disclosed in claim 9 as compositions with pharmaceutically acceptable carrier or diluent, meeting the limitations of claim 20.

Thus, Uhlmann et al. disclose all limitations of and anticipate claims 1-4, 11-18 and 20.

Response to arguments regarding Uhlmann et al.

Applicants argue the claims as amended are not anticipated by Uhlmann et al. The claims now require that when Q_2 is O, Q_3 is CH_3. Q_3 is the equivalent of Z or Z' in the oligonucleotides of Uhlmann et al., which are explicitly disclosed in claim 1, column 60, as including C_1-C_{18} alkyl. Therefore, the oligonucleotides disclosed by Uhlmann et al. anticipate the claims even as amended.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
April 23, 2007